

**REMARKS**

**Amendments**

Claims 8, 10 and 19 have been amended. Claims 1-7, 11-17, 20-44, 46, and 48-72 have been canceled. The amendments to the claims do not constitute new matter and are completely supported throughout the specification and originally filed claims.

The foregoing amendments are made solely to place the claims in condition for allowance in response to the final rejection, and are not intended to limit the scope of the invention. Further, the amendments to the claims are made without prejudice to the pending or now canceled claims or to any subject matter pursued in a related application. The Applicant reserves the right to prosecute any canceled subject matter at a later time or in a later filed divisional, continuation, or continuation-in-part application.

Upon entry of the amendment, claims 8-10, 18, 19, 45 and 47 are pending in the instant application.

**Formalities**

The Examiner has noted that the status of claim 52 is unclear as the status of the claim was not marked in the claim list submitted in the Amendment filed June 18, 2003. The Applicant concurs with the Examiner's conclusion that the claim has been canceled, and its status has been listed correctly in the claim list submitted with the instant Amendment.

Applicant believes that the status of all claims should be clear and accurate in this claim list.

In view of the Amendment filed June 18, 2003, the Examiner has withdrawn the 35 U.S.C. § 112, first paragraph (written description and enablement) rejection of claims 1-4, 8-10, 18, 19, 45, 47 and 52, the 35 U.S.C. § 112, second paragraph rejection of claims 1-4, 9, 10 and 23, and the 35 U.S.C. § 103 rejection of claims 8 and 10. Further, the provisional double patenting rejection of claims 18 and 19 has been withdrawn in light of the submission of a terminal disclaimer. The rejections which remain are the rejection maintained under 35 U.S.C. § 103 of claims 1-4, and the new rejection of claims 8-10, 18, 19, 45 and 47 under 35 U.S.C. § 112, second paragraph, both of which are addressed in the amendments and remarks set forth herein.

As the status of the instant Office Action has been made FINAL, Applicant has amended and/or canceled claims solely address the issues raised by the Examiner in order to place the

claims in condition for allowance. Applicant has made a genuine effort to avoid raising any issues of new matter or requiring further search or examination.

### **Rejections**

#### ***Rejection under 35 U.S.C. § 103***

Claims 1-4 stand rejected under 35 U.S.C. § 103(a) as allegedly being unpatentable over Mansour *et al.*, 1988, *Nature*, vol. 336, No. 24, pages 348-352 ("Mansour") in view of Kato *et al.*, 1994, *Gene*, vol. 145, pages 311-312 ("Kato") and Travis *et al.*, 1997, *Proc. Natl. Acad. Sci. U.S.A.*, 94:11055-11060 ("Travis"). Applicant respectfully traverses this rejection. However, in view of the cancellation of claims 1-4, Applicant submits that the rejection under 35 U.S.C. § 103 is no longer relevant.

According to the Examiner, Mansour teaches a strategy for targeted disruption of the *hprt* and proto-oncogene *int-2* in mice embryonic stem cells, and subsequent generation of knockout mice. The disclosure of Mansour specifically relates to a general method for isolating embryonic stem cells containing a targeted mutation in an endogenous gene. More particularly, Mansour teaches the targeted disruption of the *hprt* gene and the proto-oncogene *int-2* in mouse embryonic stem cells by homologous recombination using targeting constructs specific for these genes.

Kato, as characterized by the Examiner, discloses the cloning of a mouse magnesium-dependent phosphatase gene.

Travis, according to the Examiner, discloses that human magnesium-dependent phosphatase is involved in cystic fibrosis pathogenesis and asserts that human magnesium-dependent phosphatase is a good target for developing inhibitors that have therapeutic value for cystic fibrosis.

Claims 1-4 are drawn to a magnesium-dependent phosphatase gene targeting construct and a method of making the construct, wherein the construct produces a disruption that leads to phenotypes including a lung abnormality, elevated white blood cell count, increased anxiety and increased pain threshold.

As a basis of the rejection, the Examiner states that "the recitation of 'wherein the target[ing] construct when... exhibits...a phenotypic abnormality selected from the group consisting of a lung abnormality, elevated white blood cell count...' defines the intended use of the knockout construct, which does not carry patentable weight." The Examiner states that one

of ordinary skill in the art would have been motivated to knockout the expression of the magnesium-dependent phosphatase gene in a mouse to study the function of this gene and to develop specific inhibitors for this phosphatase which may be useful in treating cystic fibrosis, as suggested by the teachings of Travis. The Examiner states that one of ordinary skill in the art would have a reasonable expectation of success based on the teachings of Mansour and Kato.

Although the Applicant disagrees, and has traversed the rejection, Applicant has canceled claims 1-4, rendering the rejection moot. Therefore, withdrawal of the rejection under 35 U.S.C. § 103(a) is respectfully requested. Applicant submits that pending claims 8-10, 18, 19, 45 and 47 are not obvious in view of the cited references, as noted by the Examiner.

***Rejection under 35 U.S.C. § 112, second paragraph***

The Examiner has rejected claims 8-10, 18, 19, 45 and 47 under 35 U.S.C. § 112, second paragraph, as being indefinite for allegedly failing to particularly point out and distinctly claim the subject matter which Applicant regards as the invention.

Regarding claims 8-10, 18, 19, 45 and 47, the Examiner asserts that the recitation of “a transgenic mouse comprising a disruption in a magnesium-dependent protein phosphatase represented by SEQ ID NO:1” renders the claims indefinite. The Examiner alleges that the phrase “magnesium-dependent protein phosphatase” refers to the protein, which has been recited to be represented by a nucleic acid sequence, namely SEQ ID NO:1. Applicant has addressed the Examiner’s concerns by reciting in the pending claims the phrase “magnesium-dependent protein phosphatase gene represented by SEQ ID NO:1”. Therefore, the pending claims, as amended, overcome this aspect of the rejection.

Further, the Examiner notes a grammatical error in claim 8 (“functional protein encoded by the a magnesium-dependent protein phosphatase gene”). Applicant has amended claim 8, as required by the Examiner, to recite “functional protein encoded by the magnesium-dependent protein phosphatase gene.”

With regard to claim 10, the Examiner asserts that the claim is incomplete for omitting essential steps, such omission amounting to a gap between steps. The Examiner asserts that the omitted steps are “1) selecting the embryonic stem cell comprising a disruption in the magnesium-dependent phosphatase gene; [and] 2) further breeding the heterozygous transgenic mouse to obtain a homozygous transgenic mouse.” Applicant traverses this aspect of the rejection. Applicant submits that claim 10, as previously written, particularly points out and

distinctly claims that which Applicant regards as the invention. However, in order to place the claim in condition for allowance, Applicant has adopted the Examiner's suggestion and inserted the allegedly omitted steps as noted above. Therefore, Applicant has overcome this aspect of the rejection.

Finally, regarding claim 19, the Examiner has requested correction of the phrase "consistent a symptom" to recite "consistent with a symptom." Applicant has amended claim 19 to adopt the Examiner's suggestion.

As the amendments to the claims have addressed the concerns of the Examiner and/or adopted the suggestions of the Examiner as noted above, the rejection of pending claims 8-10, 18, 19, 45 and 47 under 35 U.S.C. § 112, second paragraph is no longer relevant. Applicant respectfully requests withdrawal of this rejection. Applicant submits that claims 8-10, 18, 19, 45 and 47 are definite and particularly point out and distinctly claim that which Applicant regards as the invention as required by 35 U.S.C. § 112.

In view of the amendments and remarks set forth above, it is believed that the claims are currently in condition for allowance, which action is respectfully requested.

Respectfully submitted,

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